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Original Research

Has anything changed in the last decade in the long-term outcome of patients with antenatal hydronephrosis?

İsa Yılmaz[1], Harun Peru[1], Metin Gündüz[2]
[1] Department of Pediatric Nephrology
[2] Department of Pediatric Surgery, Faculty of Medicine, Selcuk University, Konya, Turkey

Abstract
Aim: We tried to determine the etiological causes of antenatal hydronephrosis (AH) patients in their postnatal follow-ups in order to stress the importance of vesicoureteral reflux (VUR), to reveal the frequency of urinary tract infection (UTI) and scarred kidney in patients with hydroureteronephrosis or obstructive hydronephrosis with (VUR), and its effect on prognosis according to the degree of hydronephrosis.
Material and Methods: In this retrospective study, 251 patients diagnosed with AH were evaluated between January 2011 and January 2021. According to the renal pelvis antero-posterior (AP) diameter measurement, patients were classified into 3 groups as mild (group-1 with 121 cases, 48.2%), moderate (group-2 with 84 cases, 33.5%) and heavy (group-3 with 46 cases, 18.3%) grades. The groups were compared in terms of demographic data, laboratory results, imaging findings and prognosis.
Results: There was a significant difference in the frequency of UTI, bilateral hydronephrosis and hydroureteronephrosis between the groups (p<0.001, p=0.003, p=0.006, respectively). The incidence of pathological causes of hydronephrosis was higher in patients with bilateral hydronephrosis (p=0.040). Urinary tract infection was found to be higher in patients with hydroureteronephrosis, obstructive hydronephrosis and VUR (p=0.012, p=0.001, p=0.006, respectively). The incidence of renal scar was found to be higher in patients with hydroureteronephrosis, VUR and UTI (p=0.001, p<0.001, p<0.001). A significant difference was detected in the incidence of VUR, obstructive hydronephrosis and renal scar between the groups (p=0.002, p<0.001, p=0.006). Expectedly, the rate of surgical operation was higher in group-3 than in group-1 and 2 (p<0,001).
Discussion: In addition to the degree of antenatal hydronephrosis, the presence and bilaterality of hydroureteronephrosis are determining factors for the diagnostic imaging method and prognosis. Mild AH tends to improve spontaneously more compared to the other two groups. Patients with moderate to severe AH should be followed up for a long time with a more established approach.

Keywords
Antenatal Hydronephrosis, Long-Term Outcomes, Childhood

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Corresponding Author: İsa Yılmaz, Department of Pediatric Nephrology, Faculty of Medicine, Selcuk University, Konya, Turkey.
E-mail: drisayilmaz@hotmail.com P: +90 332 235 42 05 F: +90 332 237 60 25
Corresponding Author ORCID ID: https://orcid.org/0000-0001-8654-9173

Introduction

Antenatal hydronephrosis, which is defined as enlargement of the renal pelvis with or without the calyces, has begun to be diagnosed more frequently and early with the widespread use of perinatological follow-ups in recent years [1]. Antenatal hydronephrosis, the most common congenital anomaly, is detected in 1-4% of all pregnancies [2]. It is bilateral at a rate of 20-40%, with twice the incidence in boys compared to girls [3]. Although it is often thought to be caused by a congenital abnormality of the kidney and urinary tract (CAKUT), a specific underlying disorder could not be detected in many patients. However, it is known that the prognosis is closely related to the underlying cause, if any. On the other hand, 36-80% of AH cases resolve spontaneously at the end of pregnancy or in the first year of life [4]. Dilatation of the calyces of the renal pelvis, the presence of parenchymal atrophy are the parameters used by the Society of Fetal Urology (SFU) to grade hydronephrosis. According to this classification, the kidney is graded as grade 0-4 hydronephrosis. Another method used to evaluate antenatal hydronephrosis is renal pelvic diameter measurement [5]. Measurement of the maximum AP distance of the renal pelvis in the transverse plane is the most commonly used method to define AH [5, 6]. Among the CAKUT diagnoses that cause antenatal hydronephrosis, there are ureteropelvic junction stenosis (UPJS), ureterovesical junction stenosis (UVJS), vesicoureteral reflux (VUR), posterior urethral valve (PUV), megaureter, multicystic dysplastic kidney (MCDB), ureterocele and renal cysts [5]. However, despite ongoing advances in understanding the genetic basis and consequences of CAKUT, there is still no consensus on the clinical significance, postnatal evaluation and management of infants with AH [7,8]. In the absence of regular follow-ups in the postnatal period, there is a risk of recurrent UTI, damage to the kidney parenchyma, impaired kidney function and kidney failure sequentially [9]. Our aim in this study is to determine the etiological causes of AH patients in their postnatal follow-ups, to stress on the importance of VUR, to reveal the frequency of UTI and renal damage, and its effect on prognosis in relation with the hydronephrosis in patients with hydroureteronephrosis, obstructive hydronephrosis and VUR.

Material and Methods

Ethical approval was obtained for this study from the local ethics committee of Selcuk University Faculty of Medicine with the decision number of 2021/40. The files of the patients who applied to Selcuk University Faculty of Medicine Pediatric Nephrology Clinic were analyzed retrospectively. The demographic data of the patients were age, gender; laboratory findings of urea, creatinine, fully automatic urinalysis, urine culture; urinary system ultrasonography (US), voiding cystourethrography (VCUG) from radiological imaging; technetium-99m-labeled (Tc-99m) dimercaptosuccinic acid (DMSA), Tc-99m mercaptoacetyltriglycine (MAG-3) from nuclear imaging and urinary system surgery reports data were collected. All patients followed up with the diagnosis of AH at this time were included in the study. Patients with a follow-up period of less than 3 months or insufficient data were excluded from the study.

In the perinatological period, patients with suspected PUV, oligohydramnios or a history of severe bilateral hydronephrosis were evaluated with ultrasonography within 24-48 hours, while other AH cases were between 3 and 7 days or 4 and 6 weeks. Patients with renal pelvis AP diameter of <9 mm in postnatal ultrasonography were considered mild, patients with 9-15 mm were considered moderate, and patients with >15 mm were considered severe AH. Patients with normal initial ultrasonography scans were followed-up with 2 more ultrasonographic imagings at 6-month intervals, and patients with an AP diameter of <7 mm in the renal pelvis were graduated from the follow-up. During the follow-up period, the patients' fully automatic urinalysis, urine culture, urea and creatinine values were asked. Urine culture was taken from mid-stream urine in patients with toilet training, and by inserting a urinary catheter in patients who were not toilet trained. The results of the patients who underwent voiding cystourethrography were recorded as the presence or absence of VUR. Voiding cystourethrography was performed when the urine cultures were clean. MAG-3 results from nuclear imaging were classified as non-obstructive or obstructive dilatation, while DMSA scintigraphy results were classified as normal or scarred kidney.

Statistical Analysis

Data entry, statistical analysis and reporting procedures were conducted electronically. Descriptive analysis was performed for demographic and clinical characteristics of the patients. The distribution of data was evaluated using the one-sample Kolmogorov-Smirnov test. Data were presented as mean ± standard deviation for normally distributed continuous variables, and frequencies (percentile) for categorical variables. Values between two different groups were compared using independent samples t-test. If the data were not normally distributed, the Mann-Whitney U test was used. The x2 test was used to evaluate the differences between categorical variables. The Kruskal-Wallis test was used to compare the data of more than two groups that did not fit the normal distribution. Test results with $P < 0.05$ were considered statistically significant.

Results

Two hundred fifty-one patients were included in the study, and 310 kidneys were evaluated; 78.5% (n=197) of the patients were male and 21.5% (n=54) were female. The male/female ratio was 197/54. The demographic characteristics of the patients included in the study are shown in Table 1. The mean urea value measured at the first admission of the patients was 16 (min=4, max=128), and the creatinine value was 0.34 (min=0.12, max=2.56). UTI was detected in 80 (31.9%) patients at any time during follow-up. Four patients had an acute renal failure at the time of initial diagnosis.

According to the classification made according to renal pelvis AP diameter measurement, 121 (48.2%) patients were mild (group-1), 84 (33.5%) patients were moderate (group-2), 46 (18.3%) patients were severe grade (group-3) hydronephrosis. The details are shown in Table 2.

While pathological causes were detected in 30 (50.8%) of 59 patients with bilateral hydronephrosis, pathological causes were detected in 69 (35.9%) of 192 patients with

unilateral hydronephrosis. The incidence of pathological causes of hydronephrosis was higher in patients with bilateral hydronephrosis (p=0.040).

There was a significant difference in the frequency of UTI, bilateral hydronephrosis and hydroureteronephrosis between the groups (p<0.001, p=0.003, p=0.006, respectively).

The rate of urinary tract infection was higher in patients with hydroureteronephrosis (48.7%), patients with obstructive hydronephrosis (70.3%) and patients with VUR (66.6%) compared to those without (p=0.012, p=0.001, p=0.006, respectively).

Vesicoureteral reflux was detected in 20 (48.8%) of 41 patients with hydroureteronephrosis, and VUR was detected in 22 (10.5%) of 210 patients without hydroureteronephrosis. Vesicoureteral reflux was seen at a higher rate in patients with hydroureteronephrosis (p<0.001). The incidence of renal scar was found to be higher in patients with hydroureteronephrosis, VUR and UTI (p=0.001, (p<0.001, p<0.001, respectively).

There was a significant difference in the incidence of VUR between the groups (p=0.002). Vesicoureteral reflux rate was found to be higher in group-2 and 3 compared to group-1. A significant difference was found between the groups in the rate of obstructive hydronephrosis in the extracted MAG-3 (p<0.001). The rate of obstructive hydronephrosis was found to be higher in Group-3. In the DMSA results, a significant difference was found between the groups in the frequency of renal scarring (p=0.006). Renal scar rate was found to be higher in Group-3. Surgical operation rate was found to be higher in group-3 compared to group-1 and 2 (p<0.001). The distribution of clinical and imaging findings of the kidneys with hydronephrosis included in the study according to the groups is shown in Table 3. Two patients developed chronic kidney disease in the follow-up.

Table 1. Demographic characteristics of the patients included in the study

Gender M/F (n; %)	197 (%78,5) / 54 (%21,5)
Getting antenatal diagnosis (n; %)	167 (%66,5)
Time to first diagnosis Mean±SD (Median; min-max) (months)	1,96±1,53 (1; 1-9)
Follow-up time Mean±SD (Median; min-max) (months)	26,77±22,37 (19,00; 3-94)
Antenatal hydronephrosis grade n (%)	
Light	121 (%48,2)
Middle	84 (%33,5)
Heavy	46 (%18,3)
Bilateral AH n (%) / Unilateral AH n (%)	59 (%23,5) / 192 (%76,5)
Hydroureteronephrosis n (%)	41 (%16,3)

Table 2. Diagnostic distribution of patients with antenatal hydronephrosis by groups

	Group 1 n=121	Group 2 n=84	Group 3 n=46
Physiological Hydronephrosis (n=153)	95	49	9
Pathological Hydronephrosis (n=98)	26	35	37
Ureteropelvic junction obstruction (n=30)	3	7	20
Ureterovesical junction stenosis (n=13)	3	4	6
Vesicoureteral reflux (n=31)	11	16	4
Posteriorurethral valve (n=1)	1	-	-
Ureteropelvic junction stenosis + Vesicoureteral reflux (n=3)	-	1	2
Posteriorurethral valve + Vesicoureteral reflux (n=3)	1	1	1
Other causes* (n=17)	7	6	4

* Double collecting system, ureterocele, diverticulum, multicystic dysplastic kidney

Table 3. Distribution of imaging findings and clinical data of patients according to groups

	Group 1 n=121	Group 2 n= 84	Group 3 n= 46	p
VCUG (n=102)	33	45	24	
VUR (n=42)	14	19	9	0,002
DMSA (n=97)	37	33	27	
Renal scar (n=33)	9	12	12	0,006
MAG 3 (n=160)	55	66	39	
Obstructive (n=37)	5	11	21	<0,001
Surgery (n=54)	14	14	26	<0,001
Spontaneous recovery (n=99)	69	27	3	0,001

Discussion

Most of the existing literature on the prognosis of infants with AH consists of retrospective studies. In this study, we touched upon important aspects in terms of the pathological causes of AH, the management and prognosis of patients, of our ethnic structure, of changing technical equipment conditions and of up-to-date medical approaches over the last ten years. In line with the literature, the proportion of male patients was higher, which remains similar in the last few decades and in different societies [10]. In our study based on patient records admitted to the pediatric nephrology clinic in the postnatal period, we found that two-thirds of the patients were prenatally diagnosed. Most prospective and retrospective literature related to the subject consists of prenatally diagnosed cases. Therefore, we cannot compare our study. We interpret this prenatal diagnosis rate as a result of recent perinatal developments in our country and the increase in pregnancy follow-up rates.

The rate of self-recovery in the mild AH group was higher than in the other two groups. However, although the increased likelihood of underlying pathological causes increased among the groups, the rate was significantly higher among the kidneys in the mild AH group at 21.5%. Gökaslan et al. [11] also grouped patients as mild to moderate-heavy, and emphasized the importance of follow-up in this group in accordance with our study because urological abnormalities in the mild AH group showed a highly heterogeneous distribution. A meta-analysis involving 1,678 babies diagnosed with fetal hydronephrosis showed that CAKUT was the underlying cause of fetal hydronephrosis in a third of patients in postpartum evaluation [6]. In our study, we found CAKUT as 36.1% among all kidneys, similar to the literature. Unlike the literature, the most common anomaly detected in our study was VUR and second frequency was UPJS. Although the frequency of UPJS increases with the severity of hydronephrosis, we found that VUR, which is our most common diagnosis, is also seen at a higher rate in moderate and severe hydronephrosis groups [6]. Similar to our results in the literature, Dias et al. showed that moderate to severe-grade VUR was associated with higher grade renal-pelvic dilatation in both intrauterine and postpartum periods [12]. Passerotti et al. and Ansari et al. similarly reported increased reflux dilatation with a degree of cervical dilactation in postpartum US [13,14].

In addition, it is known that postnatal normal ultrasound imaging does not exclude VUR. Valavi et al. detected a large number (89%) of patients with mild AH had moderate to severe VUR. In that cohort, renal sonography was not a reliable method for the prediction of VUR and its severity in patients with mild postnatal AH. However, it was reliable for high grades of VUR. These authors suggested that VCUG is mandatory for all patients diagnosed with AH. In contrast, other studies suggested that VCUG is not mandatory in children with moderate or mild AH [16-18].

In addition to all this controversial literature, the frequency of UTI and the rate of VUR were higher in patients with hydroureteronephrosis on urinary ultrasonography in our study. Unlike us, Visuri et al. in their 10-year cohort determined that the incidence of UTI was higher in patients with grade 4-5 VUR in the follow-up of a total of 192 patients with hydronephrosis, hydroureteronephrosis and VUR [19]. In their studies, hydroureteronephrosis was not prominent in terms of UTI. In addition, in our study, the rate of underlying pathological diagnosis was higher in patients with bilateral hydronephrosis. Since we have determined a higher rate of renal scarring in patients with hydroureteronephrosis, urinary tract infection and VUR, we think that VCUG should be routinely performed in patients with hydroureteronephrosis and a history of UTI, regardless of the grade of AH. In other patients, this decision should be made on an individual basis. However, in our study, the necessity of imaging methods comes to the fore in this group, since we found that the obstructive pattern and surgical requirement were higher in MAG-3 in the group with severe AH. In our study, the rate of spontaneous regression decreased as the degree of AH increased, which was consistent with the literature [6,11].

Although it covered a period of 10 years, a low number of patients in our study was the limitation of our study as our center was a tertiary care clinic dealing with complicated cases in general. Due to the retrospective nature of the study, ultrasonographic imaging was performed by different radiologists, which might have led to individual measurement errors due to experience. Another limitation is that we did not retrieve all antenatal period recordings of our patients due to their retrospective nature. Therefore, we could not obtain a conclusion about the prognosis of patients with intrauterine resolution and intrauterine recovery.

Conclusion

In conclusion, the presence of hydroureteronephrosis and bilaterality, as well as the grade of AH, are determinants of the diagnostic imaging modality and prognosis. VUR should be excluded in patients with hydroureteronephrosis and UTI. Cases with mild AH tend to resolve more spontaneously than moderate and severe cases. Patients with moderate and severe AH should be followed for a long time with a more comprehensive imaging method.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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